

Supplementary tables and figures

Table S1. Eligibility criteria

Inclusion criteria:

- Double blind, parallel group randomized controlled trials (level I)
- Reported knee-specific outcomes
- Provided pre-to-post mean change (SD) or pre- (SD) and post- (SD) means
- All Kellgren-Lawrence grades
- At least 4 weeks trial duration
- At least 11 participants in the placebo arm at trial start
- Studies of hip osteoarthritis if KOA also studied.

Exclusion criteria:

- Trials of psychological treatments or strength or endurance training as main treatment
- Open or anatomy-changing surgery
- >1 type of placebo
- Placebo combined with other treatments (exception: home exercise/ paracetamol/ unchanged medication dosage from pre-trial)
- Only graphic depiction of outcomes.

Table S2. Extracted variables:

- Year of publication
- Geographical region
- Trial size
- Mean age
- Sex
- Mean body mass index
- Funding source
- Single vs multicenter trial
- Duration of follow-up
- Mean baseline value
- Pre-post change with associated SD in placebo and active treatment arms
- Outcome measure
- Rescue medications allowed (except acetaminophen or same-dosage NSAIDs)
- Home-exercise prescribed as an adjunct to placebo
- Route of placebo delivery
- Randomization ratio placebo - active treatment
- Potential conflicts of interest
- Trial registration; date of submission; date of trial start

Table S3. Study-level covariates assessed in meta-regression

- Year of publication
- Trial size (both arms)
- Loss to follow-up
- Protocol submitted to a public registry
- Mean age
- Proportion of men
- Mean body mass index
- Single- vs multicenter setting
- Funding source
- Route of administration
- Rescue medication allowed
- Ratio placebo vs active treatment
- Pain level at baseline
- Effect size of active treatment
- Length of follow-up after last treatment
- Duration of treatment

Table S4. Some characteristics of included trials

Author	Year	Measure	Sample size	Mean age	No. Men	Mean BMI	Treatment	Region	Funding	Multi-centre
Abbasifard M(a)	2025	WPain	33	59	13	28	Lavender oil	Asia	Non-com	No
Abbasifard M(b)	2025	WPain	30	57	7	28	Hemp seed oil	Asia	Non-com	No
Abou-Raya S	2012	WPain	144	69	24	28	Duloxetine	Africa	Non-com	No
Afilalo M	2010	WPain	339	58	137	35	Tapentolol	several	Com	Yes
Al-Haddad M	2022	KOOS Pain	51	58	7		Ginkgo biloba extract	Asia	Non-com	No
Alimoradi N	2023	KOOS Pain	44	47	14	29	Metformin	Asia	Non-com	No
Alqualo-Costa R	2021	WTotal	42	65	14	30	Photobiomodulation	south-america	Non-com	No
Altman RD	2009	WPain	295	61	33	109	Sodium hyaluronate	N-America	Com	Yes
Atamaz FC	2012	WPain	37	61	10	29	TENS	Asia	Non-com	Yes
Ay S	2009	Lequesne	25	58	6		PEMF	Asia	Non-com	No
Baek HI	2024	Korean Womac	50	61	13	24	Steamed ginger	Asia	Non-com	No
Baghban F	2021	WPain	38	54	0	32	L-carnitine diet	Asia	Non-com	No
Bagnato GL	2015	WPain	33	67	8	27	PEF	Europe	Non-com	No
Baltzer AW	2009	WPain	107	60	39		Autologous conditioned serum (Orthokine)	Europe	Com	Yes
Bennell KL	2021	KOOS Pain	144	62	60	30	prp	Europe	Non-com	Yes
Berenbaum F	2019	WPain	282	64	86	30	tanezumab	Europe	Com	Yes
Bhattacharyya S	2024	WPain	20	58	3	24	Homeopathic medicine	Asia	Non-com	No
Bihlet A	2020	WPain	121	-	-	-	diclofenac gel (AMZ001)	Europe	Com	No

Bihlet A	2024	WPain	142	60	53	31	SB-061, an aggrecan mimetic	Europe	Com	Yes
Bihlet AR	2024	WPain	77	61	32	30	Apocynin and paeonol	Europe	Com	Yes
Cai	2020	WPain	110	61	47	31	zoledronic acid	Australia	Non-com	Yes
Cakir S	2014	WPain	20	57	3	30	Ultrasound	Asia	Non-com	No
Cánovas F	2022	WTotal	27	41	10	25	eggshell membrane	Europe	Com	No
Chao J	2010	WPain	33	63	31		Corticosteroid Injections	N-America	Non-com	Yes
Chappell AS	2011	WTotal	128	62	21		Duloxetine	N-America	Com	No
Chevalier X	2009	WPain	129	63	41	30	Hyaluronic acid	Europe	Com	Yes
Chu J	2022	WPain	322	54	127	28	prp	Asia	Non-com	Yes
Conaghan PG	2020	WPain	80	62	15	33	Cathepsin K Inhibitor	Europe	Com	Yes
Debbi M	2011	WPain	25	71	13	29	MSM - organosulfur molecule	Europe	Non-com	No
DeCaria JE	2012	WPain	15	73	7	29	Hyaluronic acid	N-America	Non-com	No
DeLemos B	2011	WPain	202	59	63		Tramadol	N-America	Com	Yes
Diracoglua D	2009	WPain	21	56	20	31	Hyaluronic acid	Asia	Non-com	No
Dogan N	2022	WPain	30	56	0	31	Kinesio taping	Asia	Non-com	No
Dorio M	2021	WPain	21	62	2	27	PRP	S-America	Non-com	No
Draper DO	2018	WPain	31	51	16	34	Ultrasound	N-America	Non-com	No
Ebrahimi AA	2014	WPain	30	58	0	32	Elaeagnus angustifolia L. medulla powder	Asia	Non-com	No
Elik H	2020	WPain	30	60	3	31	PRP	Asia	Non-com	No
Emadedin M	2018	WPain	24	55	15	32	BMMSC	Asia	Non-com	No
Enteshari - Moghaddam A	2019	WPain	50	52	19		Methotrexate	Asia	Non-com	No
Essex MN	2012	WPain	44	58	16		NSAID	N-America	Com	Yes
Essex MN	2014	WTotal	62	62	24		NSAID	N-America	Com	No
Farid R	2010	WPain	20	-	3	-	passion fruit peel extract	Asia	Com	No
Fary RE	2011	WPain	36	69	20	27	PES	Australia	Non-com	No

Fleischmann RM	2019	WPain	85	60	33	29	lutikizumab (immunoglobulin)		Com	Yes
Fransen M	2015	WPain	151	61	29	29	Glukosamin	Other	Com	No
Frestedt JL	2008	WPain	16	59	6	32	Glukosamin (Aquamin)	N-America	Com	No
Fukuda TY	2011	KOOS Pain	23	57	0	28	Pulsed shortwave	S-America	Non-com	Yes
Furuzawa	2009	WPain	26	67	2	30	Polymerized Collagen	N-America	Non-com	No
Geusens P	2017	WPain	105	62	46	30	choline-stabilized orthosilicic acid	Europe	Com	Yes
Giombini A	2011	WPain	28	67	9	27	Microwave diathermy	Europe	Non-com	No
Gundog M	2012	WPain	12	61	3	29	Interferential Current Therapy	Asia	Non-com	No
Görmeli G	2017	IKDC	43	53	20	30	PRP	Asia	Non-com	No
Hancke JL	2019	WPain	36	56	9	27	Andrographis paniculata extract	S-America	Com	Yes
Hangody L	2018	WPain	69	58	18	29	Hyaluronic acid	Europe	Com	Yes
Hashemzadeh K	2020	WPain	40	54	4		Nanocurcumin	Asia	Non-com	No
Henrotin Y	2019	KOOS Pain	45	63	11	29	curcumin	Europe	Com	Yes
Henrotin Y	2022	WPain	70	53	25	27	Rubus idaeus extract	Europe	Com	No
Herrero-Beaumont G	2016	WPain	78	67	13	28	Glukosamin	Europe	Com	Yes
Hewlings S	2019	WPain	44	53	13	28	chicken eggshell membrane hydrosylate	N-America	Com	No
Holt RJ	2015	WPain	246	62	87	33	NSAID	N-America	Com	Yes
Hsieh RL	2012	KOOS Pain	35	61	7	26	Monochromatic Infrared Energy	Asia	Non-com	No
Huang TL	2011	WPain	100	64	22	25	Hyaluronic acid	Asia	Non-com	Yes
Huber R	2010	WPain	44	64	12	27	Articulatio Genus D5 (AG5), a cartilage preparation	Europe	Com	No
Hudson B	2021	WPain	103	65	43	31	Nortriptyline		Non-com	No

Hunter DJ	2022	WPain	26	65	7	28	dexamethasone sodium phosphate	Asia	Com	Yes
Huseini HF	2022	WPain	58	63	13	29	Methotrexate	Asia	Non-com	No
Jacquet A	2009	WPain	40	58	12		Phytalgic® (fish-oil, vitamin E, Urtica dioica)	Europe	Com	No
Jesus C	2015	pain	35	70	5		Ozone in air	S-America	Non-com	Yes
Jin X	2016	WPain	204	63	102	30	d-vitamin	Australia	Non-com	Yes
Jin Y	2018	WPain	76	59	18	30	Calcitonin gene-related peptide blockade	Other	Com	Yes
Jokar M	2013	WPain	26	48	1	25	Hydroxychloroquine	Asia	Non-com	No
Jubb RW	2008	WPain	32	66	8	30	Acupuncture	Europe	Non-com	No
Kakuo S	2018	JKOM	26	54	17		Psidium guava leaf extract	Asia	Com	No
Kanzaki N	2011	JKOM	20	58	3	23	Chondroitin, Glucosamine	Asia	Com	No
Kapci Yildiz S	2015	Lequesne	30	58	4	31	Pulsed ultrasound	Asia	Non-com	No
Karakas A	2020	WPain	48	61	4	29	pulsed ultrasound	Asia	Non-com	No
Karlsson J	2009		80	62	27		Naproxcinod	Europe	Com	No
Kaya Mutlu E	2017	WPain	21	57	2	31	Kinesio taping	Asia	Non-com	No
Ke Y	2021	WPain	220	61	48	25	Hyaluronic acid	Asia	Com	Yes
Khamevar A	2021	WPain	30	71	6	30	Pistacia atlantica gum	Asia	Non-com	No
Kim KI	2023	WPain	130	64	26	26	AD-MSCs	Asia	Non-com	Yes
Kingsbury SR	2024	WPain	78	60	29	34	Methotrexate	Europe	Non-com	Yes
Kumar B	2025	WPain	40	47	21	26	Boswellian extract	Europe	Com	No
Kumar S	2015	WTotal	11	23	1	23	Collagen peptide	Asia	Com	No
Lam WC	2021	WPain	41	63	11	24	Acupuncture	Asia	Non-com	No
Lane NE	2010	WPain	75	58	32		tanezumab	N-America	Com	No
Lao L	2015	WPain	45	60	28		Chinese herbs		Non-com	Yes
Laotammateep C	2025	WPain	20	65	2	25	High Intensity Laser	Asia	Non-com	No

Laslett LL	2024	WTotal	132	62	56	30	Krill oil	Other	Non-com	Yes
Lee BW	2024	WPain	12	64	0	24	Allogeneic BM-MSCs	Asia	Non-com	No
Lei M	2017	WTotal	231	67	97	25	lactobacillus probiotic	Asia	Non-com	No
Leung YY	2018	WPain	55	59	16	29	Colchicine	Asia	Non-com	No
Lewis E	2022	KOOS total	28	60	12	30	PRP	Australia	Com	No
Li L	2025	WPain	36	56	13		Herbal Formulation	N-America	Com	No
Lin KY	2019	WTotal	27	62	10	25	PRP	Asia	Non-com	No
Lin LL	2018	WPain	21	60	1	25	Acupuncture	Asia	Non-com	No
Lopresti AL	2022	KOOS Pain	50	58	24	29	Curcumin		Com	Yes
Lozada CJ	2017	WPain	111	60	30	46	Multicomponent homeopathic products	N-America	Com	Yes
Lugo JP	2016	WTotal	62	53	28	24	Deer Bone Extract		Com	Yes
Mahboob N	2009	WPain	25	-	-	-	Topical Gel (Lake Urmia Mud)	Asia	Non-com	No
Mahler EAM	2019	WPain	28	68	15	26	low-dose radiation therapy	Europe	Non-com	No
Majeed M	2019	Womac Total	24	58		23	Herbs	Asia	Com	No
McAlindon TE	2017	WPain	70	57	32	32	corticosteroids	NA	Non-com	No
McAlindon TE	2013	WPain	73	63	33	31	Vitamin D	N-America	Non-com	Yes
Migliore A	2021	Lequesne	345	64	115	29	Hyaluronic acid	Europe	Com	Yes
Mitchell PG	2022	WPain	57	52	27	26	oil extract Epiitalis	Asia	Com	Yes
Mohsenzadeh A	2023	WPain	45	57	4		Cutan herb oil	Asia	Com	No
Møller I	2023	WTotal	28	57	12	30	Specialized pro-resolving mediators (SPMs) oil	Europe	Com	Yes
Möller I	2010	lequesne	65	61	24		Chondroitin	Europe	Com	No
Nelson FR	2014	WTotal	26	62	8	34	Hyaluronic acid	N-America	Com	No
Nguyen C	2024	Womac function	70	63	20	28	Resvaratrol	Europe	Non-com	Yes
Nishida Y	2021	WTotal	220	62	75	26	Hyaluronic acid	Asia	Com	No

Nishida Y	2020	WTotal	89	-	21	25	Hyaluronic acid	Asia	Com	No
Notarnicola A	2011	Lequesne	30	60	10		Methylsulfonylmethane and boswellic acid	Europe	Non-com	No
Oben J	2009	Lequesne	20	-	-	-	Phellodendron and Citrus extracts	N-America	Com	No
Panahi Y	2014	WPain	26	58	5	30	curcuminoid	Asia	Non-com	No
Patel S	2013	WPain	26	53	6	26	PRP	Asia	Non-com	No
Petersen KKS	2022	WPain	25	65	7	28	Duloxetine	Europe	Com	No
Pettersen SC	2018	WPain	184	59	79	30	Hyaluronic acid	N-America	Com	Yes
Prior MJ	2014	WPain	275	62	79		Extended release acetaminophen	N-America	Com	Yes
Rabini A	2015	WTotal	25	75	8	-	Muscle vibration	Europe	Non-com	No
Radnovich	2017	WPain	59	61	19	30	Cryotherapy	N-America	Com	Yes
Rattanachaiyanont M	2008	WPain	60	63	0	26	short wave diathermy	Asia	Non-com	No
Reginster JY	2017	Lequesne	205	65	53	31	Glukosamin	Europe	Com	No
Reginster JY	2012	WPain	559	62	135	30	Strontium ranelate	Europe	Com	Yes
Reichenbach S	2021	WPain	112	66	52	27	TNS	Europe	Com	Yes
Roman-Blas JA	2017	WPain	78	67	13	28	Glucosamine sulfate	Europe	Com	Yes
Rondanelli M	2019	WTotal	30	63	10	28	Non-Animal Chondroitin Sulfate	Europe	Com	No
Ross M	2024	WPain	21	58	9	31	Autologous protein	Other	Non-com	No
Ruff KJ	2009	WPain	31	-	-	-	Natural Eggshell Membrane	N-America	Com	Yes
Sadri B	2023	WTotal	20	56	2	29	AD-MSCs	Asia	Non-com	No
Salimzadeh A	2017	KOOS Pain	55	56	6	30	black cumin (Iranian traditional medicine)	Asia	Non-com	No
Salimzadeh A	2018	WPain	39	-	0	32	Garlic supplement	Asia	Non-com	No
Sampalis JS	2012	WPain	15	55	6		UP446 (anti-inflammatory agent of botanical origin)	N-America	Com	No
Sanghi D	2013	WPain	53	53	21	26	Vitamin D	Asia	Non-com	No

Sawitzke AD	2022	WPain	65	64	58	32	Pulsed Low-Intensity Ultrasonography	N-America	Non-com	No
Schauss AG	2012	WTotal	40	54	15		Collagen	N-America	Com	No
Schnitzer T	2019	WPain	232	60	75		tanezumab	N-America	Com	Yes
Schnitzer T	2011	WPain	260	60	33	33	Naproxcinod	N-America	Com	Yes
Schnitzer T	2023	WTotal	234	63	71		anti-catabolic (ADAMTS-5) inhibitor	many	Com	Yes
Schwappach J	2017	WPain	20	61	29	7	Human serum albumin (LMWF-5A)	N-America	Com	No
Selfe TK	2008	WPain	19	65	7	32	Neurostimulation	N-America	Non-com	No
Sengupta K	2008	WPain	25	52	5	26	Boswellia extract	N-America	Com	No
Sengupta K	2010	WPain	20	52	9	25	Boswellia extract	Asia	Com	No
Shanahan EM	2023	WPain	31	66	9		Genicular Nerve Block	Australia	Non-com	No
Shin D	2018	Wpain	30	60	9	24	Deer Bone Extract	Asia	Non-com	No
Shine BK	2025	WPain	50	64	5	23	Latilactobacillus sakei capsules	Asia	Com	No
Shiojima Y	2023	JKOM	32	62	7	22	undenatured type II collagen	Asia	Com	Yes
Shoara R	2015	WPain	33	52	4		Chamomile oil	Asia	Non-com	No
Shrestha R	2018	WPain	85	67	0	23	Triamcinalone	Asia	Noncom	No
Sihvonen R	2013	Lysholm	76	52	47	28	Arthroscopic meniscectomy	Europe	Non-com	No
Simon LS	2009	WPain	157	62	65		topical diclofenac solution	N-America	Com	No
Smith PA	2016	WPain	15	47	6	27	Plasma	N-America	Com	No
Snijders	2011	WPain	116	59	41	30	Doxycycline	Europe	Non-com	No
Spierings LH	2013	WPain	141	57	49		tanezumab	N-America	Com	Yes
Stonehouse	2022	WPain	118	56	54	28	Krill oil	australia	Com	Yes
Suarez-Almazor ME	2010	WPain	151	65	54		Acupuncture	N-America	Non-com	No
Suzuki Y	2016	JKOM	25	64	4	24	Krill oil	Asia	Com	No
Sønmez DZ	2024	WPain	36	59		9	St. John's Wort Oil	Asia	Noncom	No
Taheri M	2023	KOOS Pain	50	55	8	29	Squill oxymel	Asia	Non-com	No

Takeuchi F	2022	JKOM	25	50	4	23	Non-Essential Amino Acids	Asia	Non-com	No
Tantavisut S	2017	WPain	35	69	9	27	Vitamin E	Asia	Non-com	No
Tashiro T	2012	JKOM	30	69	7		Hyaluronic acid	Asia		No
Toguchi A	2023	JKOM	44	49	11	23	Methylsulfonylmethane	Asia	Com	No
Tsuji T	2015	WPain	25	67	6	24	Glukosamin	Asia	Com	No
Ulus Y	2012	WPain	20	60		31	Ultrasound	Asia	Non-com	No
Uysal A	2020	WPain	52	62	9	31	ESWT	Asia	Non-com	No
Vaidya N	2025	WPain	30	55	10	25	Boswellia gum resin	Asia	Com	No
van der Weegen W	2014	WTotal	97	60	50	29	Hyaluronic acid	Europe	Com	No
Varenna M	2015	WTotal	34	67	18	26	bisphosphonate (neridronate)	Europe	Non-com	No
Vishal AA	2011	WPain	30	55	11	25	Aflapin (derived from Boswellia serrata gum resin)	Asia	Non-com	No
Wang SJ	2021	WPain	23	61	6	26	Hyaluronic acid	Asia	Com	No
Wang Z	2020	WPain	34	62	13	31	Curcuma extract	Australia	Com	No
Wei XY	2025	WTotal	28	60	8	25	Acupuncture	Asia	Non-com	No
Wu Q	2024	WPain	65	61	26	23	high plant protein/peptide nutrition supplementation	Asia	Non-com	No
Wu YT	2018	WPain	20	63	5	24	Saline	Asia	Non-com	No
Yang KGA	2008	WTotal	78	53	43	28	Autologous interleukin-1 receptor antagonist	Europe	NR	Yes
Yavuz U	2012	Lequesne	30	60	11		Corticosteroid	Asia	Non-com	No
Yip	2008	WPain	18	74	5	-	massage with aromatic Ginger essential oil	Asia	NR	No
Zegels B	2013	Lequesne	117	65	38	29	Chondroitin	Europe	Com	Yes
Zhang YF	2021	WTotal	14	62	6	25	ESWT	Asia	Com	No
Zhao J	2016	WPain	20	61	4	31	Chinese herbal medicine	Asia	Non-com	No

Zhao L 2021	2021	WPain	191	63	50	25	Laser Moxibustion	Asia	Non-com	No
Zhao Z 2013	2013	WPain	31	62	11	26	ESWT	Asia	Non-com	No
Zhong Z	2019	WPain	31	63	12	25	ESWT	Asia	Non-com	No

Legend. Wpain, WOMAC pain; Wtotal, WOMAC total; KOOS, The Knee injury and Osteoarthritis Outcome Score; JKOM, Japanese Knee Osteoarthritis Measure; ESWT, extracorporeal shockwave therapy; PEF; pulsed electromagnetic fields; PRP, platelet-rich plasma; ADMSC, adipose derived mesenchymal stem cell; IKDC, International Knee Documentation Committee.

Table S5. Univariate analysis. Covariates significantly associated with effect size

<u>Covariate</u>	Coefficient (SE)	2-sided p-value	R² analogue
Funding source (commercial vs non-commercial)	0.33 (0.07)	<0.0001	0.22
Effect size in treatment arm	0.16 (0.03)	<0.0001	0.14
Region (N-America vs other)	0.41 (0.19)	0.01	0.09
Level of pain at baseline (% of worst)	0.68 (0.32)	0.03	0.09
Allowed rescue medication	0.13 (0.12)	0.04	0.05
Sample size (placebo arm)	0.0007 (0.0002)	0.002	0.02

Table S6ab. Sensitivity analysis

a. Effect size (Hedges' g) according to risk of bias in each domain

<u>Risk of bias</u>	<u>Randomization</u>	<u>Allocation concealment</u>	<u>Performance</u>	<u>Detection</u>	<u>Reporting</u>	<u>Loss To F/U</u>	<u>Sample size</u>
High (n)	0.50 (17)	0.61 (34)	0.64 (55)	0.60 (28)	0.63 (54)	0.69 (53)	0.61 (53)
Some concerns (n)	0.54 (28)	0.61 (34)	0.55 (36)	0.60 (59)	0.57 (69)	-	-
Low (n)	0.68 (136)	0.66 (113)	0.68 (90)	0.68 (94)	0.58 (0.72)	0.62 (128)	0.65 (128)
p-value	0.20	0.82	0.36	0.57	0.30	0.42	0.66

b. Hedges' g in trials without high risk of bias in any domain (mixed effects analysis)

	<u>Hedges' g (SE)</u>
All trials (n = 179)	0.64 (0.04)
Trials without high risk in any domain (n = 34)	0.65 (0.07)

Figure S1. Risk of bias. Revised Cochrane RoB-2 tool with sample size and loss-to- followup as additional domains. Green: low risk; Yellow: some concerns; Red: high risk.

Author	Randomisation	Allocation concealment	Performance bias	Detection bias	Selective reporting	Sample size >49	Loss to followup >15%
Abbasifard M 2025a	✓	✓	!	!	✓	✗	✓
Abbasifard M 2025b	!	✗	!	!	✓	✗	✓
Abou Raya S 2012	✓	✓	!	!	✗	✓	✓
Afilalo J 2010	✓	✓	✗	✗	✓	✓	✗
Al-Haddad M 2022	✓	!	!	!	✓	✓	✗
Alimoradi N 2023	✓	✓	✓	✓	✗	✗	✓
Alqualo-Costa R 2021	✓	✓	!	✓	✗	✓	✗
Altman 2009	✓	!	✗	!	!	✓	✓
Atamaz FC 2012	!	✓	✗	✗	!	✓	✓
Ay, S 2009	✗	✗	!	✓	!	✓	✓
Baek HI 2024	✓	✓	✓	✓	✓	✓	✓
Baghban F 2021	✓	!	✓	✓	!	✓	✓
Bagnato GL 2015	✓	✓	✓	✓	✗	✓	✓
Baltzer AW 2009	!	!	✗	✗	!	✓	✓
Bennell KL 2021	✓	✓	✓	✓	✓	✓	✓
Berenbaum F 2019	✓	✓	✓	✓	!	✓	✗
Bhattacharyya S 2024	✓	✓	✓	✓	✓	✗	✓
Bihlet A 2020	✓	✓	✗	!	✓	✓	✓
Bihlet A 2024	✓	✓	✗	!	✗	✓	✓
Bihlet A 2024b	✓	✓	✓	✓	✗	✓	✓
Cai G 2020	✓	✓	✓	✓	✓	✓	✓
Cakir S 2014	✓	!	!	!	!	✗	✓
Cánovas F 2022	!	!	✓	✓	!	✓	✓
Chao J 2010	!	✗	✗	!	!	✓	✓
Chappell AS 2011	✓	✓	✗	✗	✗	✓	✓
Chevalier X 2009	✓	!	✗	!	✗	✓	✓
Chu J 2022	✓	✓	✓	✓	!	✓	✓
Conaghan PG 2020	✓	✓	✓	✓	✗	✗	✓
Debbi EM 2011	✗	✗	!	!	!	✓	✓
DeCaria JE 2012	✓	✗	!	!	!	✗	✗
DeLemos B 2011	✗	✗	✗	✗	!	✓	✗
Diracoglou D 2009	✓	!	✗	!	!	✓	✓
Dogan N 2022	✗	✓	✗	✗	✓	✗	✗
Dorio M 2021	✓	✓	!	!	✗	✗	✓
Draper DO 2018	✓	✓	!	✓	✓	✓	✓
Ebrahimi AA 2014	✓	✓	!	!	✓	✗	✓
Elik H 2020	✓	✗	✗	✗	!	✓	✓
Emadedin M 2018	!	✗	!	!	!	✗	✓
Enteshari -Moghaddam A 2019	!	✓	✗	!	!	✓	✓

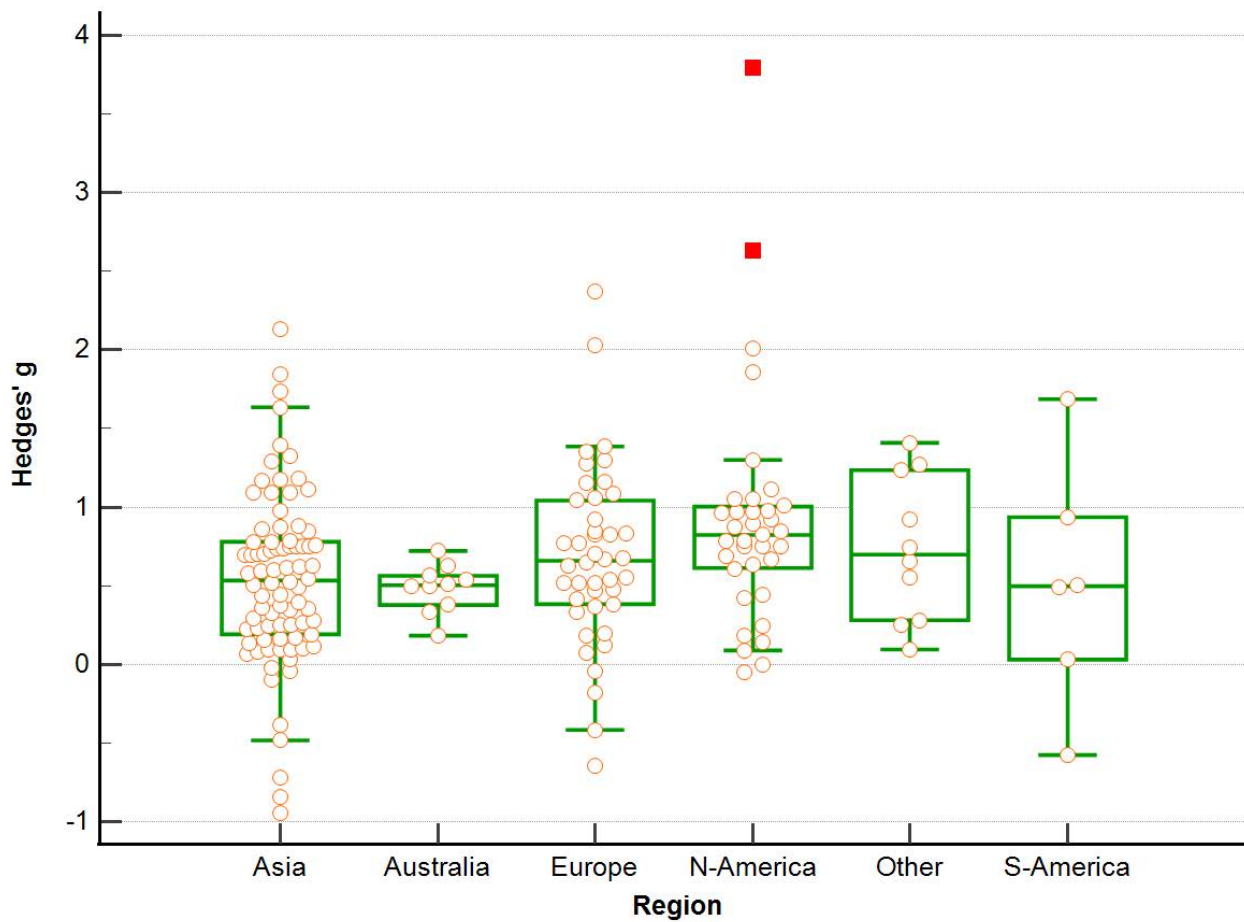
Essex MN 2012	✓	✗	✗	✗	!	✓	✗
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Farid R 2010	✗	✗	✓	✓	!	✗	✗
Fary RE 2011	✓	✓	✓	✓	✓	✓	✓
Fleischmann RM 2019	✗	✗	!	!	✓	✓	✗
Fransen M 2015	✓	✓	✓	✓	✓	✓	✗
Frestedt JL 2008	✓	!	✓	✓	✗	✗	✗
Fukuda TY 2011	✗	✓	✗	✗	!	✗	✗
Furuzawa CK 2009	✓	✗	✓	✓	!	✓	✓
Geusens P 2017	✓	✓	✓	✓	✗	✓	✗
Giombini A 2011	✓	✓	✗	!	!	✓	✓
Gundog M 2012	!	✗	✗	✗	!	✗	✓
Görmeli G 2017	✓	✓	✗	!	!	✓	✓
Hancke JL 2019	✓	✓	✓	✓	✓	✓	✓
Hangody L 2018	✓	✓	!	!	✓	✓	✓
Hashemzadeh K 2020	!	✓	✓	✓	✓	✗	✓
Henrotin Y 2019	✓	✓	✓	✓	✗	✓	✗
Henrotin Y 2022	✗	✗	✗	✗	✗	✓	✓
Herrero-Beaumont G 2016	✓	✓	!	!	✗	✓	✗
Hewlings S 2019	✗	✗	!	!	!	✓	✓
Holt RJ 2015	✓	✓	✓	✓	✓	✓	✓
Hsieh RL 2012	✓	✓	✗	✗	!	✓	✓
Huang TL 2011	✗	✗	✗	!	✗	✓	✓
Huber R 2010	✓	✓	!	!	!	✓	✓
Hudson B 2021	✓	✓	!	!	!	✓	✓
Hunter DJ 2022	✓	✓	✗	!	✓	✓	✗
Huseini HF 2022	✓	✓	!	!	✓	✓	✓
Jacquet A 2009	!	✗	!	!	✗	✓	✓
Jesus C 2015	✓	✓	✓	✓	✓	✓	✓
Jin X 2016	✓	✓	✓	✓	✓	✓	✗
Jin Y 2018	✓	✓	✓	✓	✓	✓	✗
Jokar M 2013	✓	✗	✓	✓	✓	✗	✓
Jubb RW 2008	!	✗	✗	✗	!	✓	✓
Kakuo S 2018	!	✗	✓	✓	!	✓	✓
Kanzaki N 2011	✓	✓	✓	✓	!	✗	✓
Kapci Yildiz S 2015	✗	✗	✗	✗	✗	✗	✓
Karakas A 2020	✓	✗	✗	✗	✗	✓	✗
Karlsson J 2009	✓	✓	✓	✓	!	✓	✗
Kaya Mutlu E2017	✓	✓	✗	✗	!	✓	✗
Ke Y 2021	✓	✓	✗	!	✓	✓	✓
Khamevar A 2021	✓	✓	!	!	✗	✓	✓
Kim KI 2023	✓	✓	✓	✓	✗	✓	✓
Kingsbury SR 2024	✓	✓	✓	✓	!	✗	✓
Kumar B 2025	✓	✓	✓	✓	✓	✗	✓
Kumar S 2015	✓	✗	!	!	!	✓	✓
Lam WC 2021	✓	✓	✗	!	✓	✓	✓
Lane NE 2010	✓	✓	✗	✗	✗	✓	✗
Lao L 2015	✓	✓	✓	✓	✗	✓	✓

Laotammateep C 2025	✓	✓	✗	✗	✗	✗	✓
Laslett LL 2024	✓	✓	✓	✓	!	✓	✗
Lee BW 2024	✓	✓	✗	✗	✓	✗	✓
Lei M 2017	✓	!	✓	✓	!	✓	✓
Leung YY 2018	✓	✓	✓	✓	✗	✓	✓
Lewis E 2022	✓	✓	✗	!	✓	✓	✓
Li L 2025	✗	✗	✓	✓	✗	✗	✓
Lin KY 2019	✓	!	✗	!	!	✓	✓
Lin LL 2018	✓	✓	✗	!	✗	✗	✓
Lopresti AL 2022	✓	✓	✓	✓	✓	✓	✓
Lozada 2017	✓	✓	✓	✓	✓	✓	✗
Lugo JP 2016	✓	✓	✓	✓	✓	✓	✓
Mahboob N 2009	!	!	✗	✗	!	✓	✓
Mahler EAM 2019	✓	✓	✓	✓	!	✓	✓
Majeed M 2019	✓	✓	✓	✓	✗	✗	✗
McAlindon 2013	✓	✓	✓	✓	✓	✓	✗
McAlindon TE 2017	✓	✓	!	✓	✓	✓	✓
Migliore A 2021	✓	✓	✗	!	✓	✓	✓
Mitchell PG 2022	✓	✓	✓	✓	✓	✗	✓
Mohsenzadeh A 2023	✗	✗	✗	✗	✗	✓	✗
Möller I 2010	✓	✗	!	!	✓	✓	✗
Møller I 2023	✗	✗	✗	✗	✗	✓	✓
Nelson FR 2014	✓	✓	✓	✓	!	✗	✗
Nguyen C 2024	✓	✓	✓	✓	✓	✗	✓
Nishida Y 2020	✓	✓	✗	!	!	✓	✓
Nishida Y 2021	✓	✓	✗	!	✓	✓	✓
Notarnicola A 2011	✗	✗	!	!	!	✓	✓
Oben J 2009	✓	!	✓	✓	!	✗	✗
Panahi Y 2014	!	!	✓	✓	!	✗	✗
Patel S 2013	✓	!	✗	✗	!	✓	✓
Petterson SC 2018	!	✗	✗	!	✗	✓	✓
Prior MJ 2014	✓	✓	✓	✓	✗	✓	✓
Rabini A 2015	!	✓	✗	✗	✓	✗	✓
Radnovich R 2017	✓	✓	✗	✗	✓	✓	✗
Rattanachaiyanont, M 2008	✓	✓	✗	!	✗	✓	✓
Reginster JY 2012	✓	✓	✓	✓	✗	✓	✗
Reginster JY 2017	!	!	✓	✓	!	✓	✗
Reichenbach S 2021	✓	✓	✗	!	✗	✓	✓
Roman-Blas JA 2017	✓	✓	✗	✗	!	✓	✓
Rondanelli M 2019	!	!	✓	✓	✗	✓	✓
Ross M 2024	✓	✓	✓	✓	✓	✓	✓
Ruff KJ 2009	✓	✓	✓	✓	✗	✓	✗
Sadri B 2023	!	✗	!	!	✓	✓	✓
Salimzadeh A 2017	✓	!	✓	✓	✓	✓	✗
Salimzadeh A 2018	✓	!	✗	✗	✗	✗	✓
Sampalis JS 2012	!	!	!	!	!	✗	✓
Sanghi D 2013	✓	✓	✓	✓	!	✓	✓
Sawitzke AD 2022	✓	✓	✓	✓	✓	✓	✗

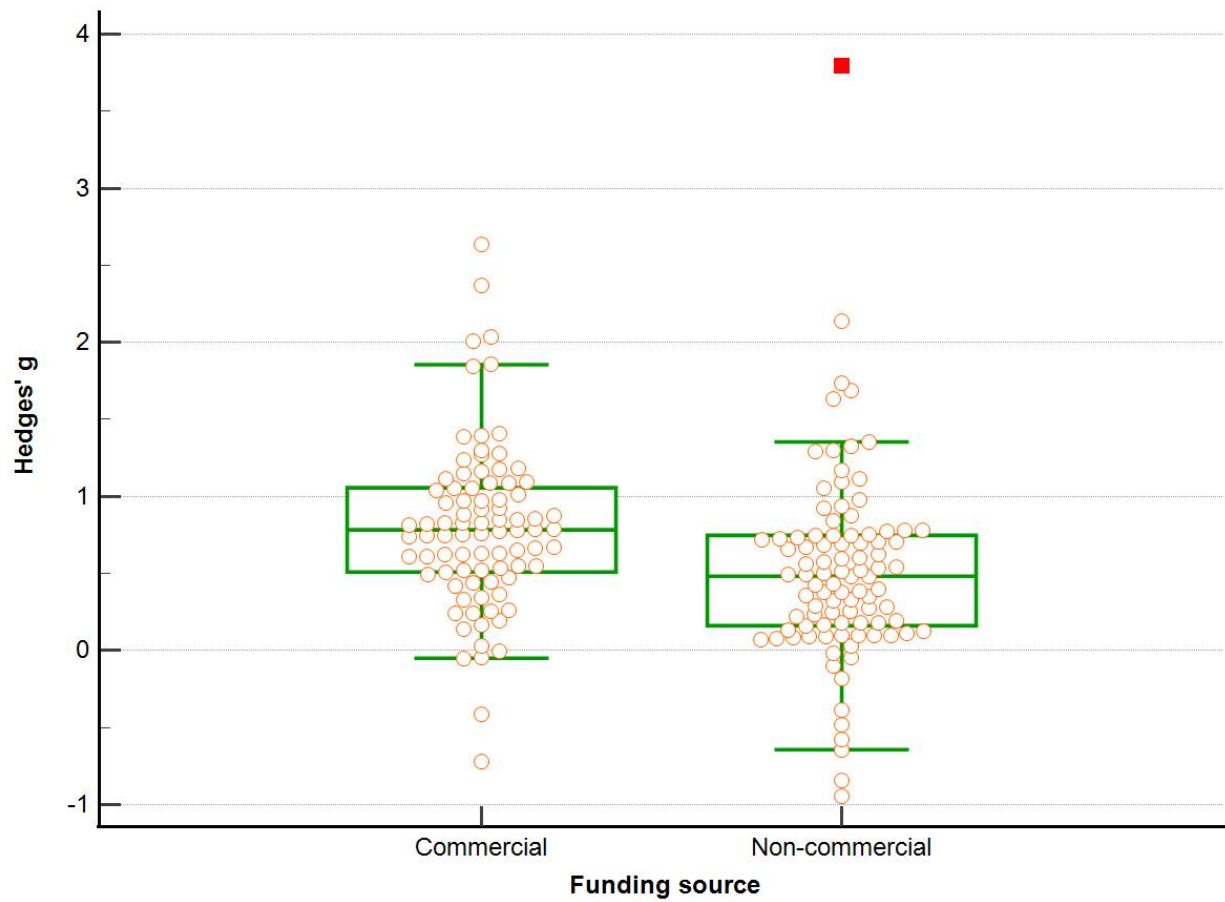
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Schwappach J 2017	✓	✓	✓	✓	✗	✗	✓
Selfe TK 2008	✓	✓	✗	!	!	✗	✓
Sengupta K 2008	✓	✓	✓	✓	✗	✗	✓
Sengupta, K 2010	✓	✓	✓	✓	✗	✗	✓
Shanahan EM 2023	✓	✓	✗	!	✓	✓	✓
Shin D 2018	✓	✓	!	!	✓	✓	✗
Shine BK 2025	✗	✗	✓	✓	✗	✗	✓
Shiojima Y 2023	✓	✓	✓	✓	!	✓	✓
Shoara, R 2015	✓	✓	!	!	✗	✓	✗
Shrestha 2018	✓	✓	!	!	!	✓	✗
Sihvonen R 2013	✓	✓	✓	✓	✓	✗	✓
Smith PA 2016	✓	✓	✓	✓	!	✗	✓
Snijders GF 2011	✓	✓	!	!	✓	✓	✓
Stonehouse W 2022	✓	✓	✓	✓	✓	✓	✗
Suarez Almazor ME 2010	✓	✓	✓	✓	✗	✓	✓
Suzuki Y 2016	!	✓	✓	✓	✓	✗	✓
Sønmez D 2024	!	✗	✗	!	✗	✓	✗
Taheri M 2023	✗	✗	✗	✗	✗	✗	✓
Takeuchi F 2022	✓	✓	✓	✓	!	✓	✓
Tantavisut S 2017	✗	!	✓	✓	✗	✗	✓
Tashiro T 2012	!	!	✓	✓	!	✓	✓
Toguchi A 2023	✗	✗	✓	✓	!	✗	✗
Tsuji T 2015	✓	✓	✓	✓	!	✗	✗
Vaidya N 2025	✗	✗	!	✗	✓	✗	✓
van der Weegen W 2014	✓	!	✓	✓	!	✓	✓
Varenna M 2015	✓	✓	✓	✓	✓	✓	✗
Vishal AA 2011	✓	✓	✓	✓	✗	✓	✓
Wang SJ 2021	✓	✓	✓	✓	✗	✗	✓
Wang SJ 2021	!	!	!	!	✗	✗	✗
Wang Z 2020	✓	✓	✓	✓	✓	✓	✓
Wei XY 2025	✓	✗	✗	✗	✗	✗	✓
Wu Q 2024	✓	✓	✓	✓	✗	✗	✓
Yang KGA 2008	✓	✓	!	!	!	✓	✓
Yavuz U 2012	!	!	✗	!	!	✓	✓
Yip YB 2008	!	✗	✗	✗	!	✗	✓
Zegels B 2013	✓	✓	✓	✓	✓	✓	✓
Zhang YF 2021	✓	✓	✗	✗	✓	✗	✗
Zhao J 2016	✓	✓	!	!	!	✓	✓
Zhao L 2021	✓	✓	✓	✓	✗	✓	✓
Zhao Z 2013	✓	!	✗	✗	!	✓	✗

Figure S2a-d. Regression of Hedges' g on covariates contributing to explained variance.

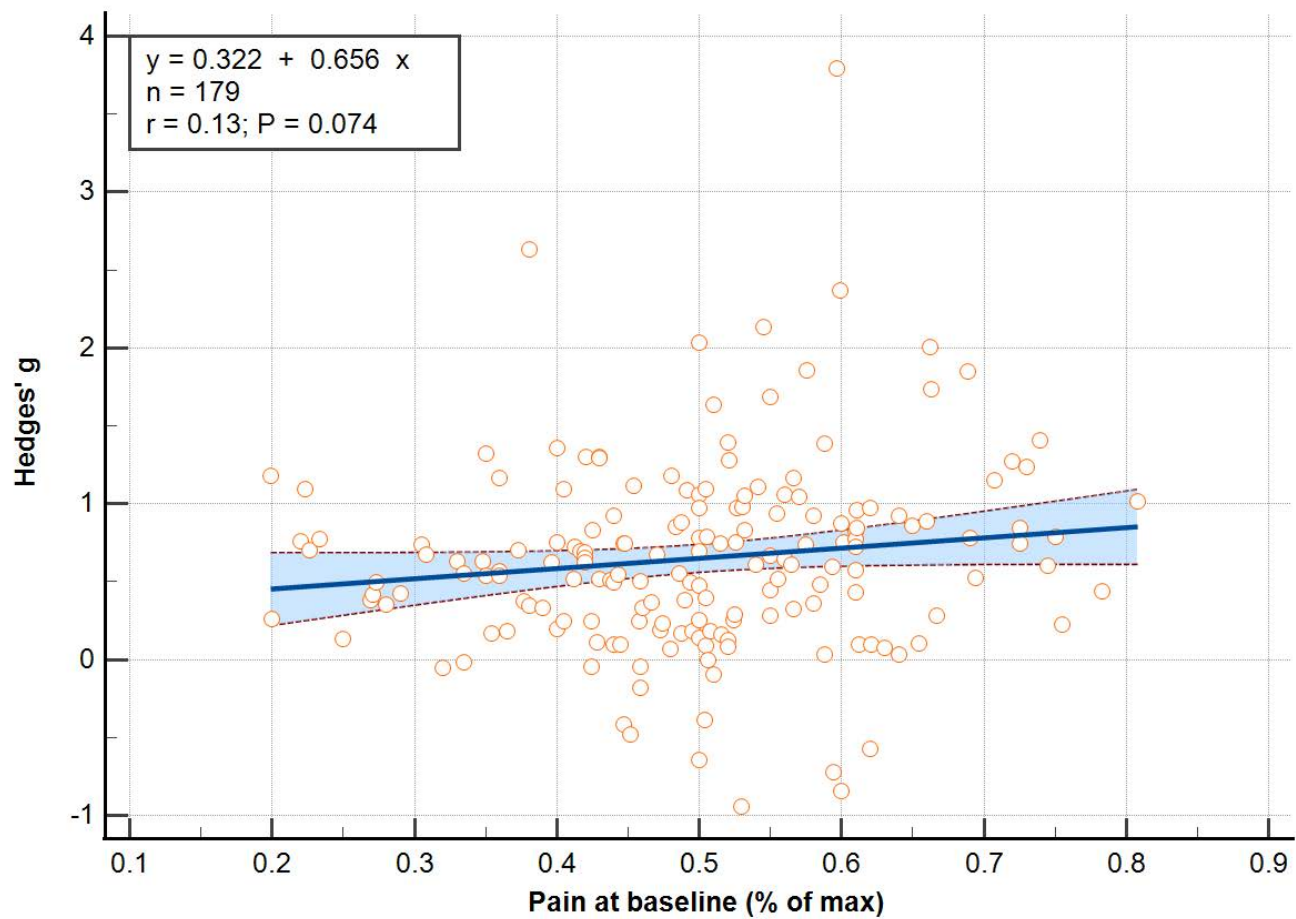
a) Geographic region



b) Funding source



c) Pain at baseline (proportion of of worst possible)



d) Effect size (Hedges' g) in active treatment arm.

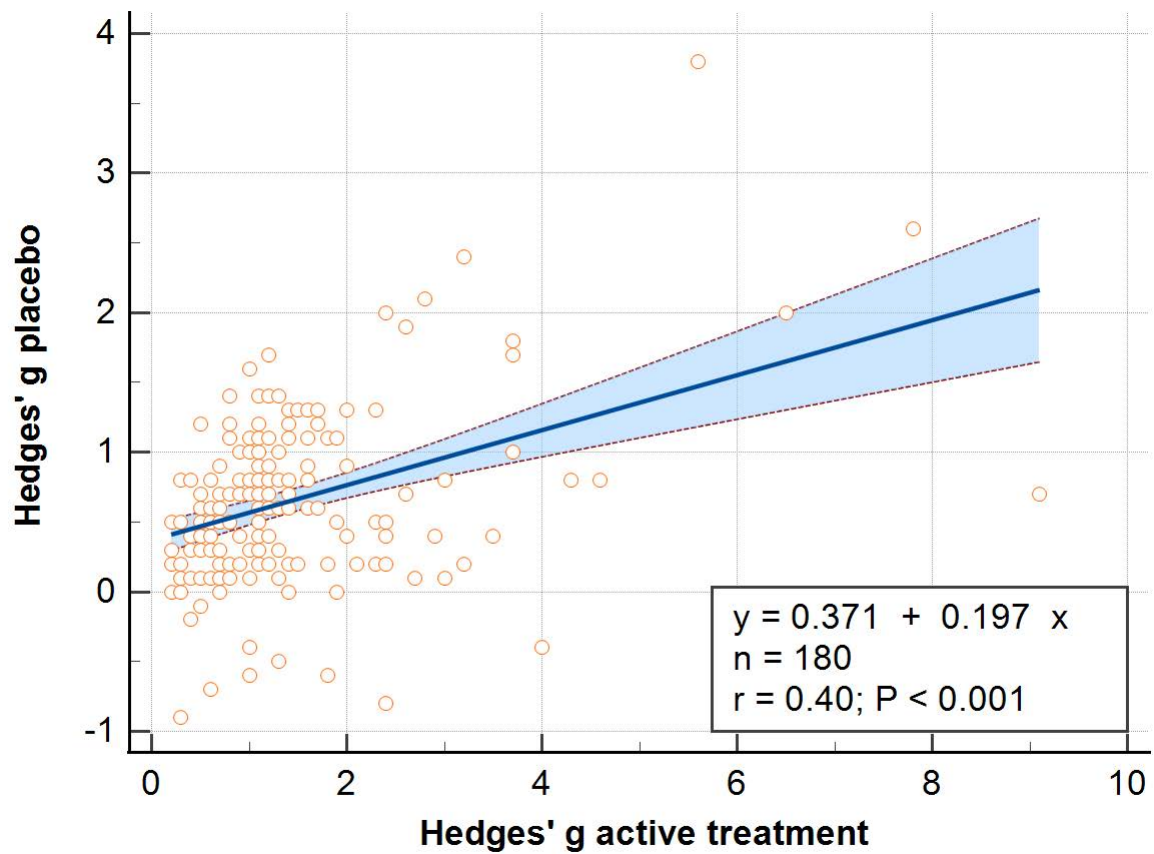
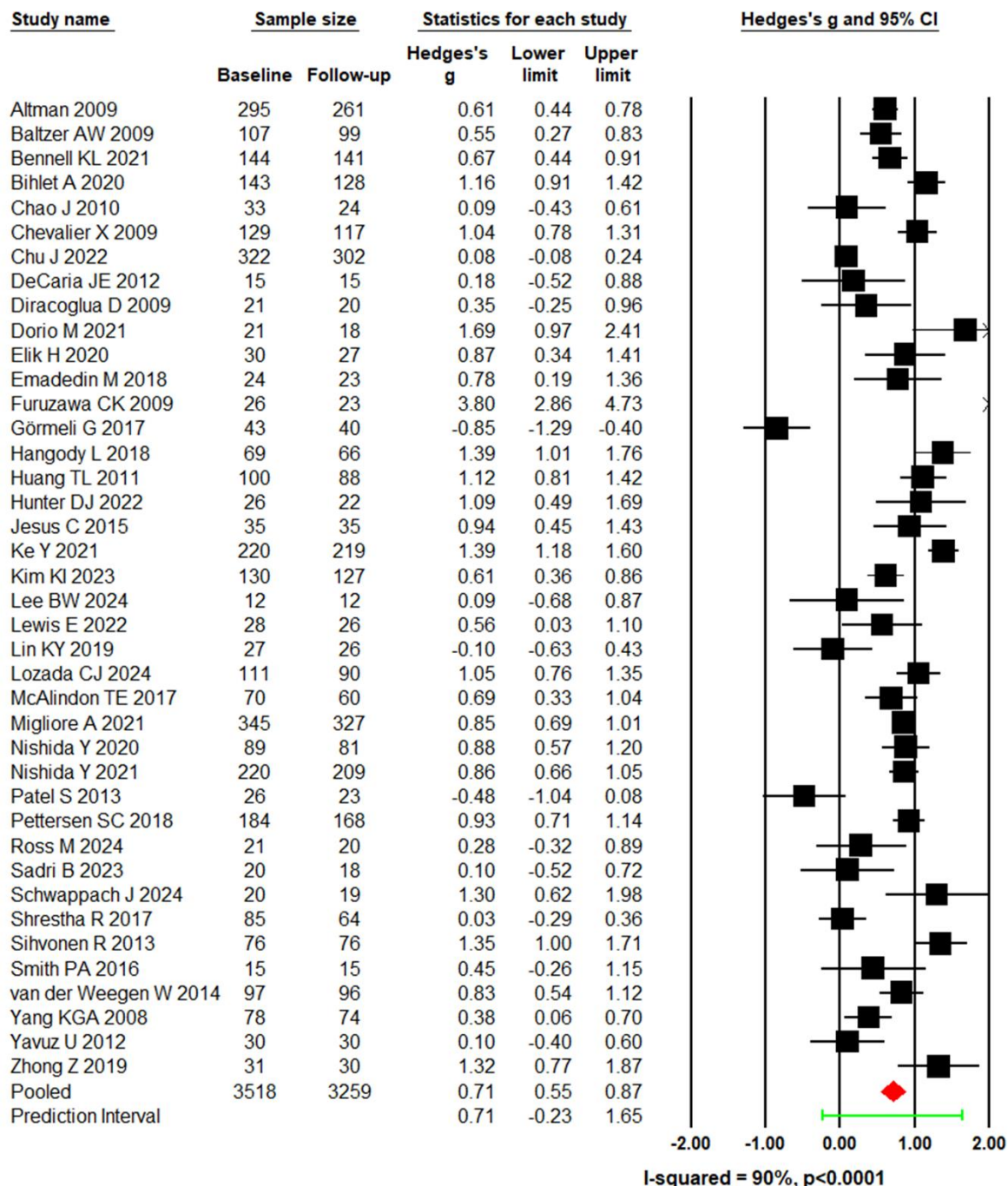
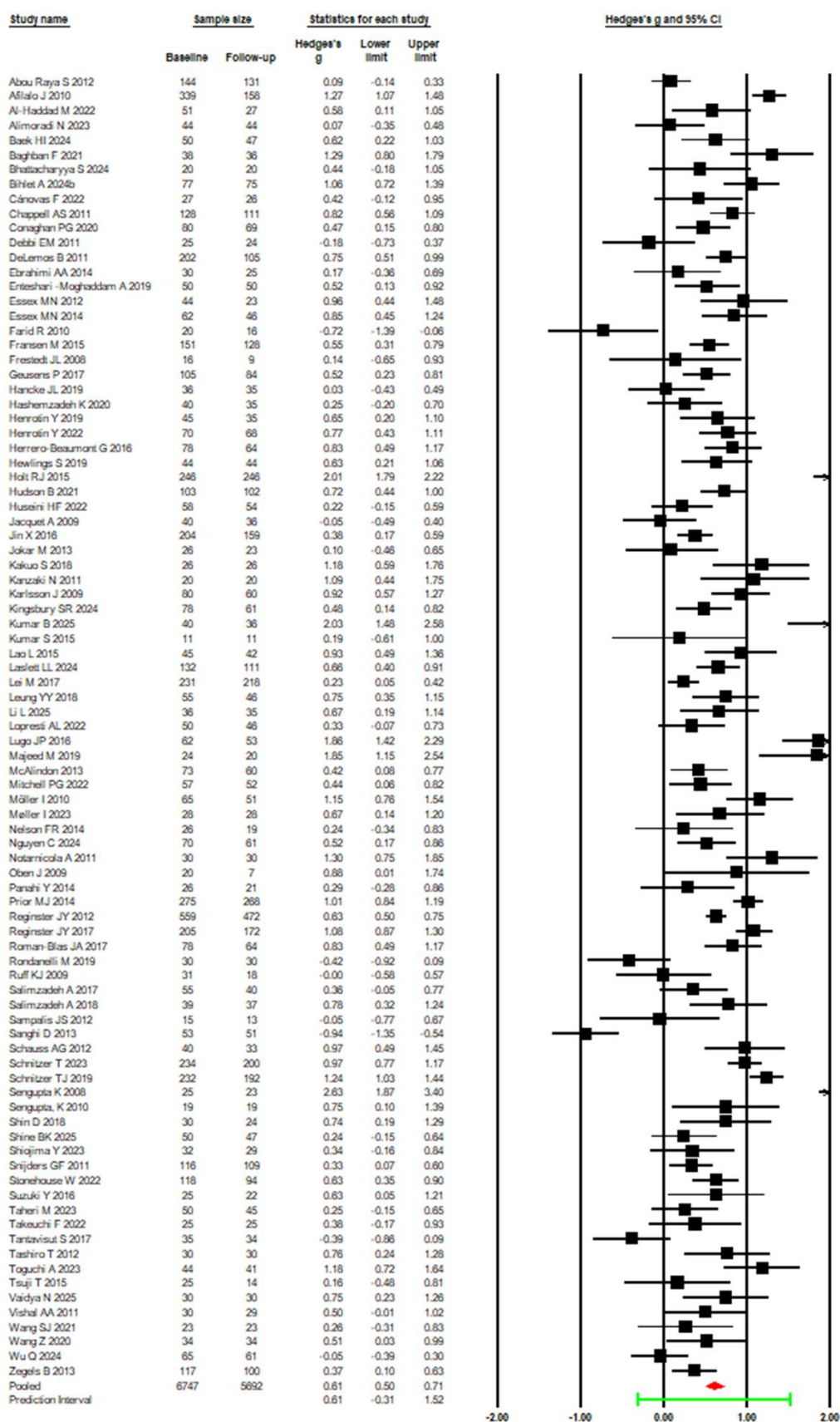


Figure S3a-e. Forest plot analyses. Hedges'g by route of placebo delivery.

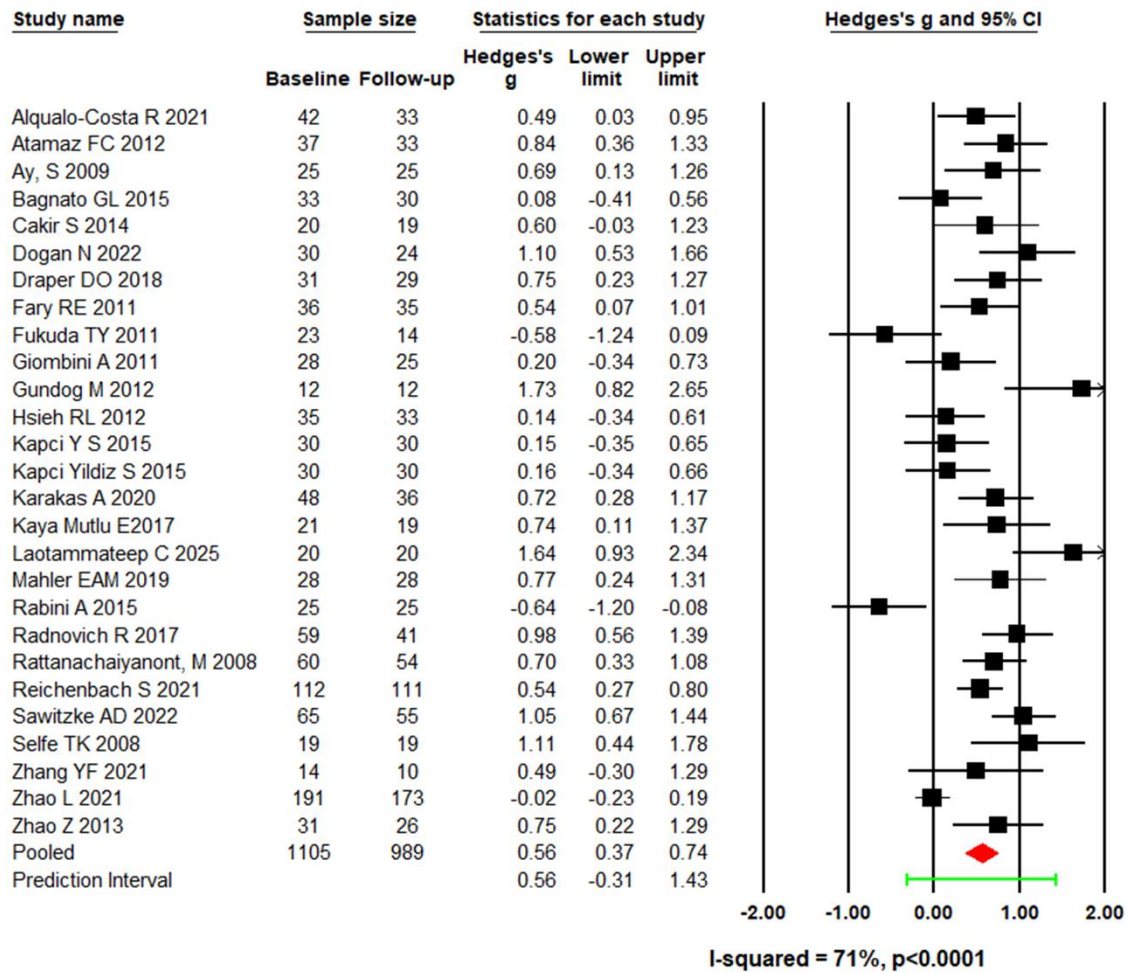
Horizontal bars: 95% confidence intervals. Red diamonds: pooled values. Green lines: prediction interval.



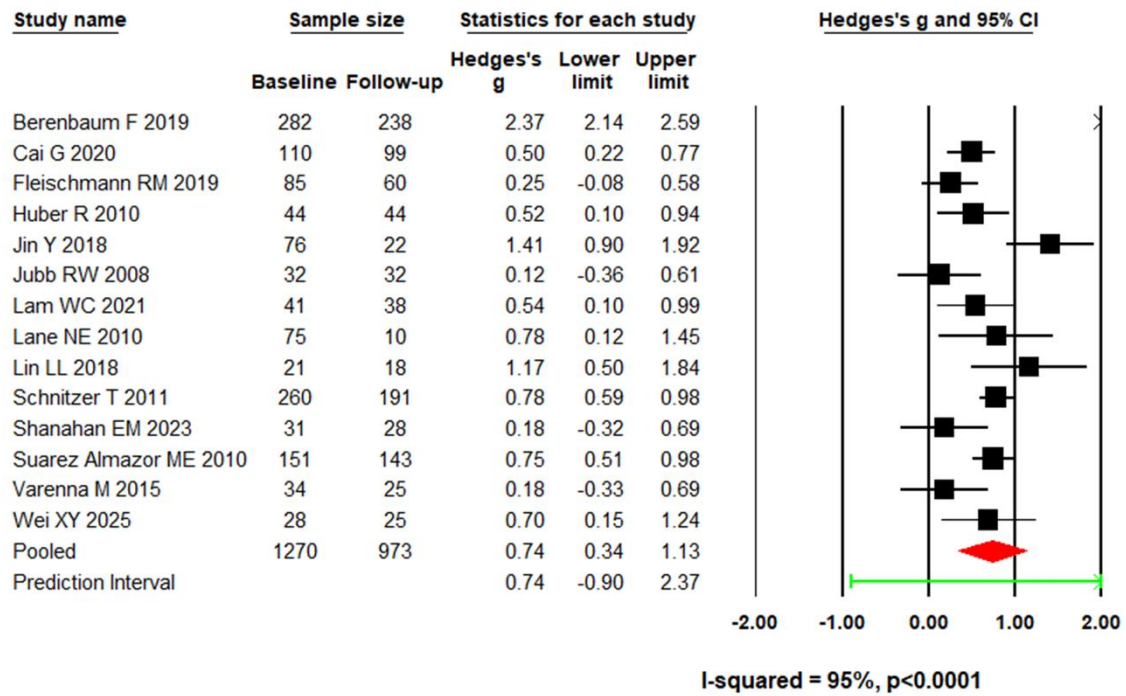
b. Oral (tablets, capsules, syrup etc)



c. Physical (laser, ESWT, ultrasound, taping etc)



d. Subcutaneous/ intravenous/ intradermal (including acupuncture)



e. Topical (gel, ointment etc)

